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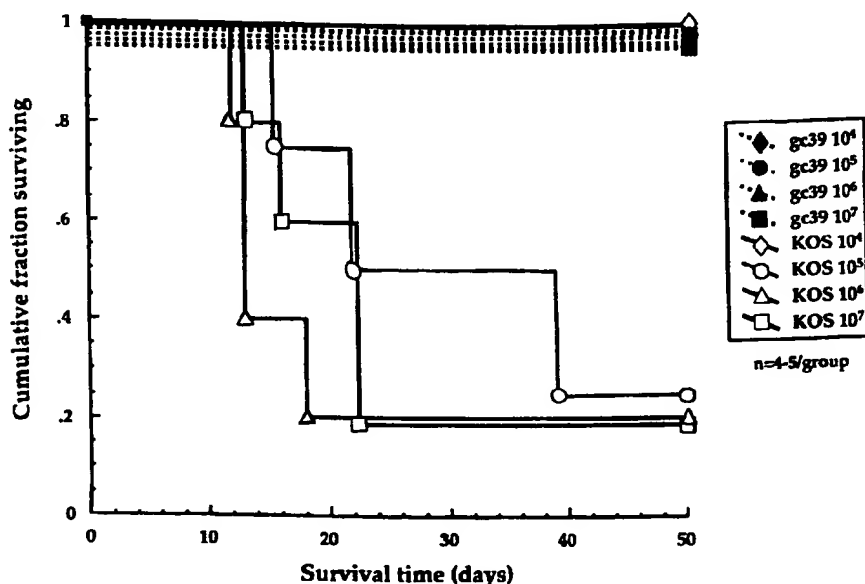
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- (71) Applicant: **ONYX PHARMACEUTICALS, INC.** [US/US]; 3031 Research Drive, Richmond, CA 94806 (US).
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18 October 2001

[Continued on next page]

(54) Title: **HERPES SIMPLEX VIRUS-1 GLYCOPROTEIN C MUTANTS FOR TREATING UNWANTED HYPERPROLIFERATIVE CELL GROWTH**



(57) Abstract: The present invention relates to pharmaceutical compositions, kits, and methods of use thereof, comprising, a mutant human herpes simplex virus, which is cytopathic to susceptible target cells, such as neoplastic cells. Preferably, the virus does not produce a functionally active wild-type gC polypeptide coded for the UL44 gene.

IN THE CLAIMS:

1. A method for treating a neoplasm comprising cells, comprising:
administering to said neoplasm an amount of a mutant human herpes simplex virus
5 which is oncolytic to cells in said neoplasm, wherein said virus does not produce a
functionally active wild-type glycoprotein C polypeptide.
2. A method of claim 1, wherein said virus comprises a deletion in the UL44 gene
which codes for glycoprotein C.
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3. A method of claim 1, wherein said virus comprises a deletion of amino acids 33-
123 in the UL44 gene.
4. A method of claim 2, wherein said comprises an insertion in the UL44 gene which
15 codes for glycoprotein C.
5. A method of claim 1, wherein the parental strain of said virus is KOS.
6. A method of claim 1, wherein said virus is gC-39.
20
7. A method of claim 1, wherein said virus is impaired in its ability to infect, or attach
to the surface of, cells as compared to the wild-type parental strain.
8. A method of claim 1, wherein said virus is impaired in its ability to infect neuronal
25 cells as compared to the wild-type parental strain.
9. A method of claim 1, wherein said cancer is an adenocarcinoma.

10. A kit comprising a mutant human herpes simplex virus which is oncolytic to cells in a neoplasm, wherein said virus does not produce a functionally active wild-type glycoprotein C and a chemotherapeutic agent.

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11. A pharmaceutical composition comprising a mutant human herpes simplex virus wherein said virus does not produce a functionally active wild-type glycoprotein C polypeptide coded for by the UL 44 gene, and a sterile physiologically balanced solution.

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12. A pharmaceutical composition as described in claim 11 wherein said mutant human herpes simplex virus is present at 10^4 – 10^{12} pfu.

13. A pharmaceutical composition as described in claim 12 further comprising a chemotherapeutic agent.

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INTERNATIONAL SEARCH REPORT

Int. l. Application No
PCT/US 00/34621

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K39/245 C07K14/035 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, EPO-Internal, PAJ, BIOSIS, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SUNSTRUM J C ET AL: "PATHOGENICITY OF GLYCOPROTEIN C NEGATIVE MUTANTS OF HERPES SIMPLEX VIRUS TYPE 1 FOR THE MOUSE CENTRAL NERVOUS SYSTEM" VIRUS RESEARCH, vol. 11, no. 1, 1988, pages 17-32, XP000999553 ISSN: 0168-1702 cited in the application	11,12
Y	abstract page 18, paragraph 2 -page 19, paragraph 2 page 22, paragraph 3; table 1 page 25, line 1 --- -/--	1-10,13

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LUBINSKI JOHN ET AL: "In vivo role of complement-interacting domains of herpes simplex virus type 1 glycoprotein gC." JOURNAL OF EXPERIMENTAL MEDICINE, vol. 190, no. 11, 6 December 1999 (1999-12-06), pages 1637-1646, XP000999849 ISSN: 0022-1007	11,12
Y	abstract page 1637, column 1, paragraph 2 page 1638, column 1, paragraphs 1,2; figure 1 page 1639, column 1, paragraph 3 page 1641, column 1, paragraph 3 page 1643, column 1, paragraph 2 -page 1644, column 1, paragraph 2 -----	1-10,13
X	US 5 728 379 A (MIYATAKE SHIN-ICHI ET AL) 17 March 1998 (1998-03-17) cited in the application	11-13
Y	abstract column 1, line 14-21 column 4, line 51-66 column 7, line 30-35 column 22, line 65 -column 23, line 3 column 27, line 18-41 column 28, line 15-26 -----	1-10

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/34621

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1 to 9 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Int. Application No

PCT/US 00/34621

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